Clinical Case Report

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Pituitary insufficiency following traumatic thoracic injury in an adolescent male patient

A case report and literature review

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Abstract

Rationale: Traumatic thoracic injuries in adolescents are rare but could be connected with traumatic brain injuries (TBI) and development of chronic hypopituitarism. Early recognition of these endocrine problems is a significant challenge to clinicians. We present difficulties in diagnosis of hypothalamic-pituitary insufficiency following traumatic thoracic injury in adolescence. We also review the literature of similar cases.

Patient concerns: We present a case of a 24-years-old male. In 2007, at the age of 15 he underwent a severe traffic accident followed by thoracic injury with concussion, hemothorax and dissection of the aorta requiring aortic stent-graft implantation.

Diagnoses: During the post-traumatic period, transient polydipsia and polyuria symptoms were observed. The patient had no medical history of any serious disease before the accident, his growth and pubertal development was normal. After the accident the patient did not undergo any routine medical check-ups. In 2013 gonadal axis deficiency was diagnosed during investigation of libido problems. Following the diagnosis testosterone replacement therapy was initiated.

Interventions: Further endocrinological investigation was carried out in 2016. The patient's main complaints were decreased mood and poor physical fitness. BMI was 27.34 kg/m^2, with a tendency to abdominal fat distribution. The patient's height is 160 cm, while Mid Parental Height (MPH) is 173.5 cm. Decreased bone density was found in DEXA examination. Serum growth hormone level (GH) was normal while insulin-like growth factor-1 (IGF-1) level was below normal. Insulin tolerance test (ITT) and low levels of IGF-1 confirmed somatotropic axis deficiency. Nuclear magnetic resonance (NMR) of the hypothalamo-pituitary region showed no abnormalities. PROP 1 and other common genetic mutations associated with GH deficits were excluded. Testosterone treatment was continued. The patient increased physical activity and implemented diet.

Outcomes: The patient has lost weight, improved physical activity performance and is feeling better. The procedure to start GH supplementation is now in process.

Lessons: Based on our case and available literature we suggest that adolescent patients after traumatic brain injuries may require precise investigation and strict monitoring due to the possibility of unrecognized hypopituitarism.

Abbreviations: ACTH = adrenocorticotropic hormone, BMI = body mass index, CABG = coronary artery bypass grafting, CT = computed tomography, DEXA = dual energy x-ray absorptiometry, DI = diabetes insipidus, FSH = follicle-stimulating hormone, fT3 = free triiodothyronine, fT4 = free thyroxine, GHD = growth hormone deficiency, GH = growth hormone, GHRH = growth hormone-releasing hormone, GnRH = gonadotropin-releasing hormone, HHD = hypothalamo-hypophysial dysfunction, IGF-1 = insulin-like growth factor 1, ITT = insulin tolerance test, LH = luteinizing hormone, MPH = mid parental height, NMR = nuclear magnetic resonance, SAH = subarachnoid hemorrhage, TBI = traumatic brain injury, TSH = thyroid-stimulating hormone.

Keywords: central diabetes insipidus, growth hormone deficiency, hypogonadotropic hypogonadism, posttraumatic hypopituitarism, traumatic brain injury

1. Introduction

Traumatic thoracic injuries in children and adolescents are rare but could be connected with other traumas such as traumatic brain injury (TBI). Falls, road accidents, and child abuse are the most common causes of TBI in children.[1–5] The particular location and special vascularization of the pituitary gland makes it notably vulnerable to damage.[6] Disabilities are found in 40% of children with moderate or severe TBI.[7] Due to various assessment methods and a limited number of patients, little is known about the prevalence of postinjury hypopituitarism in children and adolescents. Based on data in the current literature, chronic hypopituitarism after TBI is much more frequent in adult patients than it was previously thought. Approximately 11% to 69% of the patients develop pituitary insufficiency.[8,9] Growth hormone deficiency (GHD) is the most frequent pituitary

Editor: Zelena Dora.

The authors report no conflicts of interest.

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Medicine (2017) 96:44(e8406)

Received: 29 June 2017 / Received in final form: 26 September 2017 / Accepted: 30 September 2017

http://dx.doi.org/10.1097/MD.0000000000008406

Table 1

Laboratory tests*.

	Result	Norm
Sodium	139 mmol/L	136–145
Potassium	4.60 mmol/L	3.5–5.1
Calcium	2.30 mmol/L	2.15–2.55
fT3	4.41 pmol/L	3.1–6.8
fT4	13.85 pmol/L	12.0–22.0
TSH	2.00 μIU/mL	0.20–3.20
Cortisol 8^{00}	16.09 μg/dL	—
Cortisol 24^{00}	1.57 μg/dL	—
ACTH	29.0 pg/mL	6.0–56.0
LH	1.08 mIU/mL	1.70–8.60
FSH	0.79 mIU/mL	1.50–12.40
Testosterone	3.9 nmol/L	8.64–29.00
Prolactin	217.0 μIU/mL	50.0–460.0
GH	1.8 μIU/mL	0.2–10.00
IGF-1	125.0 ng/mL	235–408

ACTH = adrenocorticotropic hormone, FSH = follicle-stimulating hormone, fT3 = free triiodothyronine, fT4 = free thyroxine, GH = growth hormone, IGF-1 = insulin-like growth factor 1, LH = luteinizing hormone, TSH = thyroid-stimulating hormone.

* Performed during hospitalization in 2016 at age 24.

problem after TBI, followed by gonadotropin- and thyroid-stimulating hormone insufficiency. An early diagnosis of these delicate problems in patients following polytrauma becomes a significant challenge to clinicians. Nonspecific signs and symptoms, as well as a similarity to the neurological and psychiatric sequalae of TBI, make their recognition difficult.

2. Case presentation

We present a case report of a 24-year-old male. In 2007, when the patient was 15 years old, he underwent a severe traffic accident, followed by thoracic injury. Diagnosed with concussion, hemothorax and dissection of the descending part of the aorta, he required an aortic stent-graft implantation in the left subclavian artery. Computed tomography (CT) of the head and neck performed immediately following the accident was normal. During the posttraumatic period (up to 14–16 weeks after accident) transient polydipsia and polyuria with low urine osmolality were observed. The patient had no medical history of any serious disease before the accident. In his routine medical/pediatric check-ups during childhood and adolescence there were no abnormalities. His growth and pubertal development were normal (pubertal growth spurt had begun at the age of 11 and was normal up to the last measurement performed at the age of 15). The last complete endocrinological assessment was performed during the posttrauma hospitalization due to the diabetes insipidus: his weight was 46.5 kg, height 160 cm, his growth was normal. Pubertal development was Tanner stage IV. Thyroid and adrenal function were normal. An endocrinological control visit was scheduled; however, after the accident the patient did not show up for any routine medical check-ups. In 2013, at age of 21, the patient reported to an endocrinologist due to problems with libido and no facial hair. During subsequent evaluation, a gonadal axis deficiency was diagnosed and testosterone replacement therapy was initiated. The patient did not continue endocrinological evaluation. In 2016, the patient was invited to perform an investigation in the Department of Endocrinology. The patient's height is 160 cm (mother's 158 cm, father's 182 cm, mid parental height [MPH] is 173.5 cm). Body mass index (BMI) was 27.34 kg/m^2 with a tendency of abdominal fat distribution. His main complaints were decreased mood and poor physical fitness. All baseline test results are presented in Table 1. During the assessment of the hypophysis (performed while testosterone treatment was discontinued), no anomalies in the functioning of the pituitary-adrenal and pituitary-thyroid gland axes were found. Prolactin level was normal. Basal testosterone was low and LH and FSH were suppressed (Table 1). Upon acute GnRH test (100 mg iv) there was no response of LH and FSH to the stimulation (Table 2). Short stature with normal GH value and decreased insulin-like growth factor 1 (IGF-1) levels aroused suspicion of a somatotropic axis deficiency. An insulin tolerance test (ITT) was performed (0.1 units of insulin/kg of body weight iv).[10,11] A lack of an adequate GH response and low levels of IGF-1 confirmed an insufficiency of the somatotropic axis (Tables 1 and 3). No clinical symptoms of diabetes insipidus were observed. No abnormalities in fluid balance or osmolality of serum and urine were found either. NMR of the hypothalamo-pituitary region was performed in which no pathology was found (Fig. 1). In genetic examination, PROP 1 and other common mutations associated with GH deficits were excluded. During urological examination no abnormalities were found besides a smaller size of the testis; pubertal development was Tanner stage IV. Intramuscular testosterone supplementation (250 mg every 10 days) was continued. The patient was informed about other treatment modalities necessary to induce spermatogenesis. DEXA scan revealed decreased bone density: Z-score of right femur was −0.5 and osteopenia in L2-L4 vertebras

Table 2

Gonadotropin-releasing hormone stimulation test*.

Time	FSH [1.5–12.4]†	LH [1.70–8.60]†
−15′	<0.1 mIU/mL	0.50 mIU/mL
0′	<0.1 mIU/mL	0.49 mIU/mL
30′	<0.1 mIU/mL	0.67 mIU/mL
60′	0.11 mIU/mL	0.69 mIU/mL
120′	0.15 mIU/mL	0.81 mIU/mL
180′	0.16 mIU/mL	0.78 IU/mL

FSH = follicle-stimulating hormone, LH = luteinizing hormone.

* Performed during hospitalization at age 24.

† Normal range.

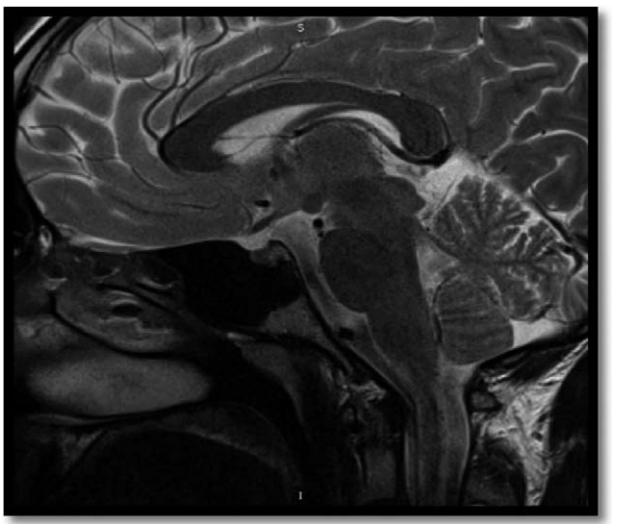

Figure 1. Pituitary NMR. NMR = nuclear magnetic resonance.

Table 3

Insulin tolerance test (ITT)*.

Time	Glucose	Growth hormone [0.2–10 μIU/mL]†
−30′	2.41 mmol/L	2.0 μIU/mL
0′	3.86 mmol/L	1.8 μIU/mL
15′	—	2.0 μIU/mL
30′	1.07 mmol/L	2.3 μIU/mL
60′	2.62 mmol/L	—
90′	3.45 mmol/L	1.6 μIU/mL
120′	—	1.2 μIU/mL

* Performed during hospitalization in 2016 at age 24.
† Normal range.

Table 4

Timeline.

Time	Patient's age	Description
May 2007	15	Car accident
May to July 2007	15	Transient polydipsia and polyuria 1.8 μIU/mL
June 2007	15	Endocrinological evaluation due to diabetes insipidus
2013	21	Diagnosis of gonadal axis insufficiency Administering of testosterone replacement therapy
December 2016	24	Diagnosis of GHD 2.3 μIU/mL

GHD = growth hormone deficiency.

with Z-score −1.4 and with the minimum Z-score value: −1.7 for L3. The patient was instructed how to increase his physical activity and implement a diet. Vitamin D (2000 μg per day) supplementation was introduced. The procedure to start supplementation with GH is now in process. The patient has since lost weight, improved his physical activity performance and is feeling better. The patient's history has been briefly presented in Table 4. The patient's informed consent has been obtained.

3. Discussion

Our case confirms that posttraumatic dysfunction of the pituitary gland in adolescents might be overlooked and diagnosed with delay due to the rarity, unspecific symptoms, and lack of regular medical check-ups. Below, we recall some studies and data related to the topic.

Einaudi et al assessed postinjury hypothalamo-hypophysial dysfunction (HHD) in pediatric patients in a retrospective and prospective study. Out of 48 patients, 5 who completed the evaluation (10.4%) developed pituitary dysfunction 6 months or more after TBI. The most common abnormality was GH deficiency.[12] The authors tried to identify risk factors associated with pituitary disorders and noticed that all patients with diagnosed HHD had lesions at CT imaging but this relationship was not observed in other studies.[8,12] However, the HHD seems to be more frequent in cases of severe and moderate TBI.[12] A lower incidence of HHD was reported by Kaulfers et al, in which 5% of the children were diagnosed with low GH response to stimulation test 1 year after TBI.[13]

In another prospective study, Personnier et al evaluated 87 children with a history of severe TBI. Among these, 6% were diagnosed with a severe GH deficit, whereas other pituitary axes were very rarely affected. The authors found no correlation between demographic and trauma characteristics and GHD. No radiological feature was associated with the disease either.[8] Similarly, in our case no abnormalities in hypothalamic-pituitary MRI have been found; however, it was performed for the first time 10 years after the accident (the CT of the head and neck performed immediately following the accident was normal). While the imaging of pituitary stalk transection confirms the cause of hypopituitarism, the extent of damage needed to induce hypopituitarism is unknown. New imaging techniques appropriately visualizing microstructural damage in the hypothalamic/pituitary region may prove useful, but for now we are fully dependent on clinical presentation and biochemical pituitary assessment.[14] The posttrauma mechanism of GH and other pituitary hormone insufficiencies is not fully understood. It may be related to hypothalamic and pituitary damage as well as to hypothalamic-portal transport of regulatory peptides. It is suggested that injury in the anterior pituitary may cause somatotroph anoxia, vascular insufficiency, and stalk injury. The hypophysial vessels and the portal capillaries in the stalk are very vulnerable to traumatic injury. Direct injury to the pituitary gland may cause anterior lobe infarction.[9]

Interesting data was presented by Casano-Sancho et al during prospective observation of children after TBI. In the group of ≥6 years, 47.8% of the children had a subnormal stimulation GH peak 3 months after TBI that persisted in 34% after 1 year. The GH response showed no correlation with injury severity. BMI increased significantly in the group with low GH response. Suboptimal cortisol was observed in 43% of the subjects, which normalized 1 year thereafter in all but 3. No clinical or hormonal abnormalities were detectable in children <6 years old. The authors suggested the prospective follow-up of children after TBI as according to their study, the impairment of pituitary function could not be predicted and to avoid the potential consequences of pituitary dysfunction.[15]

However, there are also studies where no basal pituitary disorders and no GH deficits were found in children 6.8 and 6.5 years after TBI, respectively.[16,17]

Diabetes insipidus is *common* following TBIs and pituitary surgery in adults with a prevalence ranging from 3% to 26%.[18–20] Conversely, in children and adolescents, diabetes insipidus seems to be a rare finding.[21] In a prospective study assessing 31 children after severe TBI, 10% were diagnosed with transient DI.[13] In studies performed in adults, diabetes insipidus is usually transient, and persistent DI is found in about 12% of patients evaluated 12 months after TBI.[20,22] An early diagnosis of diabetes insipidus is crucial in unconscious patients as inadequate fluid intake and related hypernatremia correspond strongly with a higher mortality rate.[23] It could also be a marker of pituitary damage and the first manifestation of a pituitary disease.[24] Our patient presented with posttraumatic transient polyuria and polydipsia which could be the first marker of hypothalamic-pituitary involvement. It was the reason for the posttrauma endocrinological evaluation and scheduled control that was not, however, continued by the patient.

In adults, Aimaretti et al observed a high risk of acquired hypopituitarism after TBI and subarachnoid hemorrhage (SAH) in evaluations conducted 3 months after brain injuries. Some abnormalities in pituitary functioning were found in 35% of TBI patients. In SAH patients, some degree of hypopituitarism was shown in 37.5%. GH deficit was the most frequent defect in both groups.[25]

In a Danish study from 2007, posttraumatic abnormalities in pituitary functioning were found in 15% of the cohort; multiple hormone deficits were observed in 6% of the patients. Trauma severity assessed with Glasgow Coma Scale score, days of intubation, and increased intracranial pressure was described as independent risk factors for the development of postinjury hypopituitarism.[26]

In one study, diffuse axonal injury and basal skull fracture found during brain imaging were connected with higher rates of hypopituitarism 1 year after TBI.[27]

Our patient had regular routine pediatric check-ups during childhood and adolescence, his growth and pubertal development were normal. The last complete endocrinological assessment was performed during the posttrauma period (as a routine pediatric medical check-up during hospitalization) and showed normal development. Endocrinological control was scheduled. Unfortunately, after the accident, during the pubertal period the patient stopped routine medical check-ups when the growth retardation and pubertal underdevelopment could have been recognized, diagnosed, and managed without delay. This confirms further that patients after TBI need scheduled clinical observation.

Clinical presentation of hypogonadism depends on the time of onset. The last routine examination at age of 15 confirmed normal pubertal development. The first clinical symptoms which made the patient visit with an endocrinologist at the age of 21 were decreased libido and a lack of facial hair. Unfortunately, no records regarding the biochemical and clinical investigation of hypogonadism were archived. During the current investigation, hypogonadism was confirmed with low testosterone, LH and FSH levels. To differentiate between hypothalamic and pituitary gonadal insufficiency, a GnRH test was performed, confirming pituitary gonadal insufficiency.[28,29]

Recent studies showed that the diagnosis of posttraumatic GHD is significantly dependent on the use of different dynamic tests and diagnostic set-up. Tests assessing GH reserves are burdened with high ratio of false-positive results.[29] It is speculated that they could cause overdiagnosing of GHD in adults. Kookshoorn et al collected data from 14 studies including 931 patients. GHRH-arginine test used to diagnose somatotropic axis insufficiency gave the prevalence of 8% to 20% (cutoff <9 μg/L); glucagon test, 11% to 39% (cutoff 1–5 μg/L); GHRH test, 2% (no cutoff); and ITT, 15% to 18% (cutoff <3 μg/L).[29] Our patient was diagnosed with ITT and the maximum level of GH was 2.3 μIU/mL, which corresponds approximately to 0.92 μg/L. Similar observations concern the diagnostics of other pituitary axes' abnormalities. A Danish study from 2014 also proved that the prevalence of GHD is strongly connected with the choice of tests and specific cutoffs, and suggested the frequency of GHD to be lower than observed previously.[30]

The presented patient underwent severe thoracic trauma followed by concussion, hemothorax, and dissection of the descending aorta. Pituitary dysfunction may have been the effect of direct mechanical damage to the hypothalamic-pituitary area. It is also not possible to exclude transient ischemia of the pituitary gland during cardiosurgery as a source. The possible apoplexy of pituitary adenomas in patients having undergone cardiac procedures was mentioned by Francis et al (but their work did not confirm a higher risk of hypopituitarism in patients without preexisting pituitary disorder[31]) and Hidiroglu, in patients after CABG.[32] There are also anecdotal reports of pituitary apoplexy following thyroidectomy,[33] lung cancer resection,[34] and cardiac gunshot in pregnant women.[35] All of these refer to patients with adenomas or enlarged pituitary glands. We have no data regarding a previous pituitary disorder in our patient. The observed abnormalities of insufficiency of the somatotropic and gonadal axes appear to be coherent with the most frequent anomalies reported in patients with postinjury hypopituitarism. The specific location in the lateral part of the pituitary gland and scarce blood supply make the somato- and gonadotropic cells more susceptible to damage.[36] Based on our case and the available data, we state that the long-term clinical and neuroendocrine assessment of patients, both adult and children, after TBIs should be considered as routine because both early diagnosis of hypopituitarism and early administration of replacement therapy have a significant influence on patients' quality of life and rehabilitation potential. Further prospective studies are required to recognize the predictive factors of hypothalamus-pituitary defects after TBIs, especially in children and adolescents.

References

[1] Masson F, Salmi LR, Maurette P, et al. Characteristics of head trauma in children: epidemiology and a 5-year follow-up. Arch Pediatr 1996;3:651–60.

[2] Lam WH, MacKersie A. Paediatric head injury: incidence, aetiology, and management. Paediatr Anaesth 1999;9:377–85.

[3] Barlow KM, Minns RA. Annual incidence of shaken impact syndrome in young children. Lancet 2000;356:1571–2.

[4] Keenan HT, Bratton SL. Epidemiology and outcomes of pediatric traumatic brain injury. Dev Neurosci 2006;28:256–63.

[5] Shao J, Zhu H, Yao H, et al. Characteristics and trends of pediatric traumatic brain injuries treated at a large pediatric medical center in China, 2002–2011. PLoS One 2013;7:e51634.

[6] Edwards OM, Clark JD. Post-traumatic hypopituitarism. Six cases and a review of the literature. Medicine (Baltimore) 1986;65:281–90.

[7] McCarthy ML, MacKenzie EJ, Durbin DR, et al. Health-related quality of life during the first year after traumatic brain injury. Arch Pediatr Adolesc Med 2006;160:252–60.

[8] Personnier C, Crosnier H, Meyer P, et al. Prevalence of pituitary dysfunction after severe traumatic brain injury in children and adolescents: a large prospective study. J Clin Endocrinol Metab 2014;99:2052–60.

[9] Tanriverdi F, Schneider HJ, Aimaretti G, et al. Pituitary dysfunction after traumatic brain injury: a clinical and pathophysiological approach. Endocr Rev 2015;36:305–42.

[10] Molitch ME, Clemmons DR, Malozowski S, et al. Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2006;91:1621–34.

[11] Biller BM, Samuels MH, Zagar A, et al. Sensitivity and specificity of six tests for the diagnosis of adult GH deficiency. J Clin Endocrinol Metab 2002;87:2067–79.

[12] Einaudi S, Matarazzo P, Peretta P, et al. Hypothalamo-hypopysial dysfunction after traumatic brain injury in children and adolescents: a preliminary retrospective and prospective study. J Pediatr Endocrinol Metab 2006;19:691–703.

[13] Kaulfers AM, Backeljauw PF, Reifschneider K, et al. Endocrine dysfunction following traumatic brain injury in children. J Pediatr 2010;157:894–9.

[14] Klose M, Feldt-Rasmussen U. Hypopituitarism in traumatic brain injury—a critical note. J Clin Med 2015;4:1480–97.

[15] Casano-Sancho P, Suárez L, Ibáñez L, et al. Pituitary dysfunction after traumatic brain injury in children: is there a need for ongoing endocrine assessment? Clin Endocrinol (Oxf) 2013;79:853–8.

[16] Moon RJ, Wilson P, Kirkham FJ, et al. Growth monitoring following traumatic brain injury. Arch Dis Child 2009;94:699–701.

[17] Heather NL, Jefferies C, Hofman PL, et al. Permanent hypopituitarism is rare after structural traumatic brain injury in early childhood. J Clin Endocrinol Metab 2012;97:599–604.

[18] Boughey JC, Yost MJ, Bynoe RP. Diabetes insipidus in the head-injured patient. Am Surg 2004;70:500–3.

[19] Maggiore U, Picetti E, Antonucci E, et al. The relation between the incidence of hypernatremia and mortality in patients with severe traumatic brain injury. Crit Care 2009;13:R110.

[20] Chowdhury T, Prabhakar H, Bithal PK, et al. Immediate postoperative complications in transsphenoidal pituitary surgery: a prospective study. Saudi J Anaesth 2014;8:335–41.

[21] Reifschneider K, Auble BA, Rose SR. Update of endocrine dysfunction following pediatric traumatic brain injury. J Clin Med 2015;4:1536–60.

[22] Agha A, Sherlock M, Phillips J, et al. The natural history of post-traumatic neurohypophysial dysfunction. Eur J Endocrinol 2005;152:371–7.

[23] Hannon MJ, Crowley RK, Behan LA, et al. Acute glucocorticoid deficiency and diabetes insipidus are common after acute traumatic brain injury and predict mortality. J Clin Endocrinol Metab 2013;98:3229–37.

[24] Marchand I, Barkaoui MA, Garel C, et al. Central diabetes insipidus as the inaugural manifestation of Langerhans cell histiocytosis: natural history and medical evaluation of 26 children and adolescents. J Clin Endocrinol Metab 2011;96:E1352–60.
[25] Aimaretti G, Ambrosio MR, Di Somma C, et al. Traumatic brain injury and subarachnoid haemorrhage are conditions at high risk for hypopituitarism: screening study at 3 months after the brain injury. Clin Endocrinol (Oxf) 2004;61:320–6.
[26] Klose M, Juul A, Poulsgaard L, et al. Prevalence and predictive factors of post-traumatic hypopituitarism. Clin Endocrinol 2007;67: 193–201.
[27] Schneider M, Schneider HJ, Yassouridis A, et al. Predictors of anterior pituitary insufficiency after traumatic brain injury. Clin Endocrinol (Oxf) 2008;68:206–12.
[28] Fleseriu M, Hashim IA, Karavitaki N, et al. Hormonal replacement in hypopituitarism in adults: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2016;101:3888–921.
[29] Kokshoorn NE, Wassenaar JE, Biermasz NR, et al. Hypopituitarism following traumatic brain injury: prevalence is affected by the use of different dynamic tests and different normal values. Eur J Endocrinol 2010;162:11–8.
[30] Klose M, Stochholm K, Janukonyté J, et al. Prevalence of posttraumatic growth hormone deficiency is highly dependent on the diagnostic set-up: results from the Danish national study on posttraumatic hypopituitarism. J Clin Endocrinol Metab 2014;99:101–10.
[31] Francis F, Burger I, Poll EM, et al. Can cardiac surgery cause hypopituitarism? Pituitary 2012;15:30–6.
[32] Hidiroglu M, Kucuker A, Ucaroglu E, et al. Pituitary apoplexy after cardiac surgery. Ann Thorac Surg 2010;89:1635–7.
[33] Kato K, Nobori M, Miyauchi Y, et al. Pituitary apoplexy after subtotal thyroidectomy in an acromegalic patient with a large goiter. Intern Med 1996;35:472–7.
[34] Yoshino M, Sekine Y, Koh E, et al. Pituitary apoplexy after surgical treatment of lung cancer. Ann Thorac Surg 2014;98:1830–2.
[35] Díaz-Gómez JL, Seigel T, Schmidt U, et al. Acute hypopituitarism in a pregnant patient after cardiac gunshot injury. J Clin Anesth 2011;23:414–7.
[36] Richmond E, Rogol AD. Traumatic brain injury: endocrine consequences in children and adults. Endocrine 2014;45:3–8.